PUBLIC HEALTH LABORATORY SERVICE
(Directed by the Medical Research Council for the Ministry of Health)

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23rd October, 1953.

Dear Dr. Lederberg,

Thank you for your letter of the 12th October.

(1) I was very glad to read in paragraph 2 of your letter the lucid discription of the transduction process, split into two phases, namely, the initial fragmentation and the subsequent adventitious carriage of the hereditary substance. In the last sentence of paragraph 2 you have contrasted this process with the role of bacteriophage in phage type determination where, as you put it, "infection with phage is not merely a necessary but also a sufficient condition of the alteration". I would like to draw your attention to the fact that the second half of the sentence I have quoted is based on a mistake. Already in the preliminary paper in Nature, 167, 603, 1951, it was shown that treatment with the same phage (f2) of five different typhoid type strains produced in each instance a different Vi-phage type. Meanwhile, you may have read the full paper in the Journal of General Microbiology, 9, 65, 1953 (August), which contains further evidence to show that the latent phages which we were able to demonstrate are not the sole factor in determination of the phage type of the organism.

Now, I hope you will not mind my asking the simple question whether it has been shown beyond doubt in transduction experiments that bacteriophage is really necessary for the 'adventitious carriage' of the hereditary material. Has it been shown conclusively that lysates heated to, say, 80°C. are no longer active in transduction? Has it been shown to your satisfaction that fragmentation of the donor organisms by other techniques (without the use of bacteriophage) does not yield equally active transducing material? It may be you have answered these questions long ago, but they occurred to me as soon as I examined Crézé's cultures and convinced myself that some of his claims were correct.

(2) Thank you for the information contained in paragraph 4 of your letter. The transfer of the typhoid H antigen d to a Salm.paratyphi B strain is certainly a spectacular achievement, although I would like to remind you of what I mentioned in my letter of the 2nd April, 1953 [on page 2, item 3 (H antigens)].

(3) I wonder whether you have laid down, for the benefit of your pupils, some rules for distinguishing between 'transduction' and '? induction' (? restoration or selection) of antigenic properties? In paragraph 4 you wrote of transduction of motility to O 901 and transfer of d to Salm. paratyphi B, both by phage little k. It seems to me advisable to lay down some rules for distinguishing between transfer of 'heterologous' antigens and restoration of the lost property to synthesize a 'homologous' antigen. Otherwise, I am afraid, one or other of your pupils may soon produce new pitfalls in addition to those already besetting Salmonella serology and phage typing.

(4) Re paragraph 2 on page 2 of your letter. - With regard to possible interference of the TVi antigen with absorption of O phage, you certainly know the paper by Nicolle et al., Ann.Inst.Past., 1953, 84, page 27. Nevertheless, it is true that typhoid cultures possessing maximal amounts of the TVi antigen are readily lysed by O phages. I would suspect interference not only with absorption, at the surface, but also with the synthesis of H antigen at the locus responsible for the development of flagella which, of course, must be very close to that responsible for the synthesis of the Vi antigen.

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(5) Agglutination by acriflavine. - I am afraid I do not know of any work, published or unpublished, relating to Sertic' claim regarding "non-specific" and "specific" H phases (C.R. Soc.Biol. 123: 951, 1936). However, I would refer you to my letter dated 26th November, 1951, when I sent you the reprint of an old paper by one of my previous co-workers, W. Hirsch, which deals with a source of error in the acriflavine test that is not generally known. As I mentioned at the time of sending the reprint, it is possible that similar sources of error may be operating in other Salmonella species and in Gram negative organisms generally, the / which possess antigens of the type of/Vi antigen of Salm.typhi.

In addition, it was also shown in that paper (J.Path. & Bact., 1937, 44, 349) that saline washings from sterile agar slopes, containing agar in colloidal form, are also flocculated by trypaflavine and modify the reaction between the bacteria and trypaflavine. It may therefore be advisable to look for similar interactions by some constituents of the particular broth or agar medium employed.

(6) Referring to your remark about the possibilities of chemical studies, following a visit by C. Weibull, I wonder what you meant by "the two sets of factors"? Did you refer to the different protein components of the various H antigens contained in the flagella, or did you think of the chemical substance, or substances, that form the transducing genetic material?

(7) Another paper by Hirsch that is probably unknown to you but may be of interest is the following: "A new bacterial variant: the non-motile H form", J.Hyg. Camb., 1947, 45, 417. You will see that this paper dealt with a hypothetical genetic factor responsible for the function or the development of the motor centre of the flagella.

I hope the two envelopes containing the old reprints have by now arrived safely.

With kind regards,

Yours sincerely,

A. Felix

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